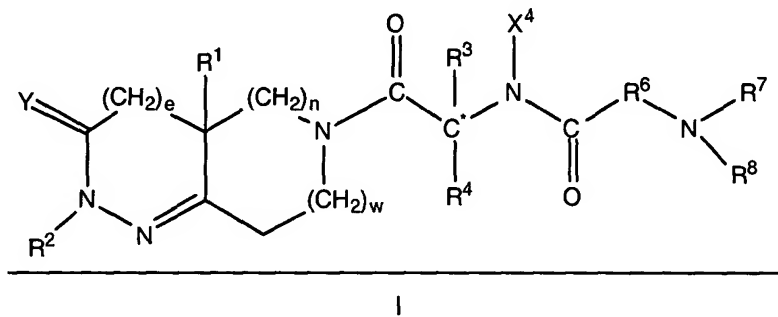


AMENDMENTS TO THE CLAIMS

Claims 1-6 (canceled)

7. (currently amended) A method for treating insulin resistance in a mammal which comprises administering to said mammal an effective amount of a compound of formula I



or the stereoisomeric mixtures, diastereomerically enriched, diastereomerically pure, enantiomerically enriched or enantiomerically pure isomers, or the pharmaceutically acceptable salts and prodrugs thereof,

wherein

e is 0 or 1;

n and w are each independently 0, 1 or 2;

provided that w and n cannot both be 0 at the same time;

Y is oxygen or sulfur;

R<sup>1</sup> is hydrogen, -CN, -(CH<sub>2</sub>)<sub>q</sub>N(X<sup>6</sup>)C(O)X<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>N(X<sup>6</sup>)C(O)(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>N(X<sup>6</sup>)SO<sub>2</sub>(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>N(X<sup>6</sup>)SO<sub>2</sub>X<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>N(X<sup>6</sup>)C(O)N(X<sup>6</sup>)(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>N(X<sup>6</sup>)C(O)N(X<sup>6</sup>)(X<sup>6</sup>), -(CH<sub>2</sub>)<sub>q</sub>C(O)N(X<sup>6</sup>)(X<sup>6</sup>), -(CH<sub>2</sub>)<sub>q</sub>C(O)N(X<sup>6</sup>)(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>C(O)OX<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>C(O)O(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>OX<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>OC(O)X<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>OC(O)(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>OC(O)N(X<sup>6</sup>)(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>OC(O)N(X<sup>6</sup>)(X<sup>6</sup>), -(CH<sub>2</sub>)<sub>q</sub>C(O)X<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>C(O)(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>N(X<sup>6</sup>)C(O)OX<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>N(X<sup>6</sup>)SO<sub>2</sub>N(X<sup>6</sup>)(X<sup>6</sup>), -(CH<sub>2</sub>)<sub>q</sub>S(O)<sub>m</sub>X<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>S(O)<sub>m</sub>(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(C<sub>1</sub>-C<sub>10</sub>)alkyl, -(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>-(C<sub>3</sub>-C<sub>7</sub>)cycloalkyl, -(CH<sub>2</sub>)<sub>q</sub>-Y<sup>1</sup>-(C<sub>1</sub>-C<sub>6</sub>)alkyl, -(CH<sub>2</sub>)<sub>q</sub>-Y<sup>1</sup>-(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup> or -(CH<sub>2</sub>)<sub>q</sub>-Y<sup>1</sup>-(CH<sub>2</sub>)<sub>t</sub>-(C<sub>3</sub>-C<sub>7</sub>)cycloalkyl;

where the alkyl and cycloalkyl groups in the definition of R<sup>1</sup> are optionally substituted with (C<sub>1</sub>-C<sub>4</sub>)alkyl, hydroxyl, (C<sub>1</sub>-C<sub>4</sub>)alkoxy, carboxyl, -CONH<sub>2</sub>,

-S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl, -CO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub>)alkyl ester, 1H-tetrazol-5-yl or 1, 2 or 3 fluoro;

Y<sup>1</sup> is O, S(O)<sub>m</sub>, -C(O)NX<sup>6</sup>, -CH=CH-, -C≡C-, -N(X<sup>6</sup>)C(O)-, -C(O)NX<sup>6</sup>-,

-C(O)O-, -OC(O)N(X<sup>6</sup>)- or -OC(O)-;

q is 0, 1, 2, 3 or 4;

t is 0, 1, 2 or 3;

said (CH<sub>2</sub>)<sub>q</sub> group and (CH<sub>2</sub>)<sub>t</sub> group may each be optionally substituted with hydroxyl,

(C<sub>1</sub>-C<sub>4</sub>)alkoxy, carboxyl, -CONH<sub>2</sub>, -S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl,

-CO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub>)alkyl ester, 1H-tetrazol-5-yl, 1, 2 or 3 fluoro, or 1 or 2 (C<sub>1</sub>-C<sub>4</sub>)alkyl;

R<sup>2</sup> is hydrogen, (C<sub>1</sub>-C<sub>6</sub>)alkyl, -(C<sub>0</sub>-C<sub>3</sub>)alkyl-(C<sub>3</sub>-C<sub>6</sub>)cycloalkyl, -(C<sub>1</sub>-C<sub>4</sub>)alkyl-A<sup>1</sup> or A<sup>1</sup>;

where the alkyl groups and the cycloalkyl groups in the definition of R<sup>2</sup> are optionally substituted with hydroxyl, -C(O)OX<sup>6</sup>, -C(O)N(X<sup>6</sup>)(X<sup>6</sup>), -N(X<sup>6</sup>)(X<sup>6</sup>),

-S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl, -C(O)A<sup>1</sup>, -C(O)(X<sup>6</sup>), CF<sub>3</sub>, CN or 1, 2 or 3 halogen;

R<sup>3</sup> is A<sup>1</sup>, (C<sub>1</sub>-C<sub>10</sub>)alkyl, -(C<sub>1</sub>-C<sub>6</sub>)alkyl-A<sup>1</sup>, -(C<sub>1</sub>-C<sub>6</sub>)alkyl-(C<sub>3</sub>-C<sub>7</sub>)cycloalkyl,

-(C<sub>1</sub>-C<sub>5</sub>)alkyl-X<sup>1</sup>-(C<sub>1</sub>-C<sub>5</sub>)alkyl, -(C<sub>1</sub>-C<sub>5</sub>)alkyl-X<sup>1</sup>-(C<sub>0</sub>-C<sub>5</sub>)alkyl-A<sup>1</sup> or

-(C<sub>1</sub>-C<sub>5</sub>)alkyl-X<sup>1</sup>-(C<sub>1</sub>-C<sub>5</sub>)alkyl-(C<sub>3</sub>-C<sub>7</sub>)cycloalkyl;

where the alkyl groups in the definition of R<sup>3</sup> are optionally substituted with

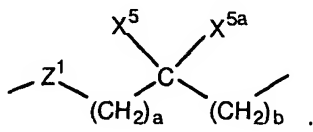
-S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl, -C(O)OX<sup>3</sup>, 1, 2, 3, 4 or 5 halogens, or 1, 2 or 3 OX<sup>3</sup>;

X<sup>1</sup> is O, S(O)<sub>m</sub>, -N(X<sup>2</sup>)C(O)-, -C(O)N(X<sup>2</sup>)-, -OC(O)-, -C(O)O-, -CX<sup>2</sup>=CX<sup>2</sup>-,

-N(X<sup>2</sup>)C(O)O-, -OC(O)N(X<sup>2</sup>)- or -C≡C-;

R<sup>4</sup> is hydrogen, (C<sub>1</sub>-C<sub>6</sub>)alkyl or (C<sub>3</sub>-C<sub>7</sub>)cycloalkyl, or R<sup>4</sup> is taken together with R<sup>3</sup> and the carbon atom to which they are attached and form (C<sub>5</sub>-C<sub>7</sub>)cycloalkyl, (C<sub>5</sub>-C<sub>7</sub>)cycloalkenyl, a partially saturated or fully saturated 4- to 8-membered ring having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur and nitrogen, or is a bicyclic ring system consisting of a partially saturated or fully saturated 5- or 6-membered ring, fused to a partially saturated, fully unsaturated or fully saturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur and oxygen;

X<sup>4</sup> is hydrogen or (C<sub>1</sub>-C<sub>6</sub>)alkyl or X<sup>4</sup> is taken together with R<sup>4</sup> and the nitrogen atom to which X<sup>4</sup> is attached and the carbon atom to which R<sup>4</sup> is attached and form a five to seven membered ring;



R<sup>6</sup> is a bond or is

where a and b are independently 0, 1, 2 or 3;

X<sup>5</sup> and X<sup>5a</sup> are each independently selected from the group consisting of hydrogen, trifluoromethyl, A<sup>1</sup> and optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl;

the optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl in the definition of X<sup>5</sup> and X<sup>5a</sup> is optionally substituted with a substituent selected from the group consisting of A<sup>1</sup>, OX<sup>2</sup>, -S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl, -C(O)OX<sup>2</sup>, (C<sub>3</sub>-C<sub>7</sub>)cycloalkyl, -N(X<sup>2</sup>)(X<sup>2</sup>) and -C(O)N(X<sup>2</sup>)(X<sup>2</sup>);

or the carbon bearing X<sup>5</sup> or X<sup>5a</sup> forms one or two alkylene bridges with the nitrogen atom bearing R<sup>7</sup> and R<sup>8</sup> wherein each alkylene bridge contains 1 to 5 carbon atoms, provided that when one alkylene bridge is formed then X<sup>5</sup> or X<sup>5a</sup> but not both may be on the carbon atom and R<sup>7</sup> or R<sup>8</sup> but not both may be on the nitrogen atom and further provided that when two alkylene bridges are formed then X<sup>5</sup> and X<sup>5a</sup> cannot be on the carbon atom and R<sup>7</sup> and R<sup>8</sup> cannot be on the nitrogen atom;

or X<sup>5</sup> is taken together with X<sup>5a</sup> and the carbon atom to which they are attached and form a partially saturated or fully saturated 3- to 7-membered ring, or a partially saturated or fully saturated 4- to 8-membered ring having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur and nitrogen;

or X<sup>5</sup> is taken together with X<sup>5a</sup> and the carbon atom to which they are attached and form a bicyclic ring system consisting of a partially saturated or fully saturated 5- or 6-membered ring, optionally having 1 or 2 heteroatoms independently selected from the group consisting of nitrogen, sulfur and oxygen, fused to a partially saturated, fully saturated or fully unsaturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur and oxygen;

Z<sup>1</sup> is a bond, O or N-X<sup>2</sup>, provided that when a and b are both 0 then Z<sup>1</sup> is not N-X<sup>2</sup> or O;

R<sup>7</sup> and R<sup>8</sup> are independently hydrogen or optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl;

where the optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl in the definition of R<sup>7</sup> and R<sup>8</sup> is optionally independently substituted with A<sup>1</sup>, -C(O)O-(C<sub>1</sub>-C<sub>6</sub>)alkyl,

-S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl, 1 to 5 halogens, 1 to 3 hydroxy, 1 to 3 -O-C(O)(C<sub>1</sub>-C<sub>10</sub>)alkyl or 1 to 3 (C<sub>1</sub>-C<sub>6</sub>)alkoxy; or

R<sup>7</sup> and R<sup>8</sup> can be taken together to form -(CH<sub>2</sub>)<sub>r</sub>-L-(CH<sub>2</sub>)<sub>r</sub>;

where L is C(X<sup>2</sup>)(X<sup>2</sup>), S(O)<sub>m</sub> or N(X<sup>2</sup>);

A<sup>1</sup> for each occurrence is independently (C<sub>5</sub>-C<sub>7</sub>)cycloalkenyl, phenyl or a partially saturated, fully saturated or fully unsaturated 4- to 8-membered ring optionally having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur and nitrogen, a bicyclic ring system consisting of a partially saturated, fully unsaturated or fully saturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur and oxygen, fused to a partially

saturated, fully saturated or fully unsaturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur and oxygen;

A<sup>1</sup> for each occurrence is independently optionally substituted, in one or optionally both rings if A<sup>1</sup> is a bicyclic ring system, with up to three substituents, each substituent independently selected from the group consisting of F, Cl, Br, I, OCF<sub>3</sub>, OCF<sub>2</sub>H, CF<sub>3</sub>, CH<sub>3</sub>, OCH<sub>3</sub>, -OX<sup>6</sup>, -C(O)N(X<sup>6</sup>)(X<sup>6</sup>), -C(O)OX<sup>6</sup>, oxo, (C<sub>1</sub>-C<sub>6</sub>)alkyl, nitro, cyano, benzyl, -S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl, 1H-tetrazol-5-yl, phenyl, phenoxy, phenylalkyloxy, halophenyl, methylenedioxy, -N(X<sup>6</sup>)(X<sup>6</sup>), -N(X<sup>6</sup>)C(O)(X<sup>6</sup>), -SO<sub>2</sub>N(X<sup>6</sup>)(X<sup>6</sup>), -N(X<sup>6</sup>)SO<sub>2</sub>-phenyl, -N(X<sup>6</sup>)SO<sub>2</sub>X<sup>6</sup>, -CONX<sup>11</sup>X<sup>12</sup>, -SO<sub>2</sub>NX<sup>11</sup>X<sup>12</sup>, -NX<sup>6</sup>SO<sub>2</sub>X<sup>12</sup>, -NX<sup>6</sup>CONX<sup>11</sup>X<sup>12</sup>, -NX<sup>6</sup>SO<sub>2</sub>NX<sup>11</sup>X<sup>12</sup>, -NX<sup>6</sup>C(O)X<sup>12</sup>, imidazolyl, thiazolyl and tetrazolyl, provided that if A<sup>1</sup> is optionally substituted with methylenedioxy then it can only be substituted with one methylenedioxy;

where X<sup>11</sup> is hydrogen or optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl;

the optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl defined for X<sup>11</sup> is optionally independently substituted with phenyl, phenoxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, -S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl, 1 to 5 halogens, 1 to 3 hydroxy, 1 to 3 (C<sub>1</sub>-C<sub>10</sub>)alkanoyloxy or 1 to 3 (C<sub>1</sub>-C<sub>6</sub>)alkoxy;

X<sup>12</sup> is hydrogen, (C<sub>1</sub>-C<sub>6</sub>)alkyl, phenyl, thiazolyl, imidazolyl, furyl or thienyl, provided that when X<sup>12</sup> is not hydrogen, X<sup>12</sup> is optionally substituted with one to three substituents independently selected from the group consisting of Cl, F, CH<sub>3</sub>, OCH<sub>3</sub>, OCF<sub>3</sub> and CF<sub>3</sub>;

or X<sup>11</sup> and X<sup>12</sup> are taken together to form -(CH<sub>2</sub>)<sub>r</sub>-L<sup>1</sup>-(CH<sub>2</sub>)<sub>r</sub>;

where L<sup>1</sup> is C(X<sup>2</sup>)(X<sup>2</sup>), O, S(O)<sub>m</sub> or N(X<sup>2</sup>);

r for each occurrence is independently 1, 2 or 3;

X<sup>2</sup> for each occurrence is independently hydrogen, optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl, or optionally substituted (C<sub>3</sub>-C<sub>7</sub>)cycloalkyl, where the optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl and optionally substituted (C<sub>3</sub>-C<sub>7</sub>)cycloalkyl in the definition of X<sup>2</sup> are optionally independently substituted with -S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl, -C(O)OX<sup>3</sup>, 1 to 5 halogens or 1-3 OX<sup>3</sup>;

X<sup>3</sup> for each occurrence is independently hydrogen or (C<sub>1</sub>-C<sub>6</sub>)alkyl;

X<sup>6</sup> is independently hydrogen, optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>2</sub>-C<sub>6</sub>)halogenated alkyl, optionally substituted (C<sub>3</sub>-C<sub>7</sub>)cycloalkyl, (C<sub>3</sub>-C<sub>7</sub>)-halogenatedcycloalkyl, where optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl and optionally substituted (C<sub>3</sub>-C<sub>7</sub>)cycloalkyl in the definition of X<sup>6</sup> is optionally independently substituted by 1 or 2 (C<sub>1</sub>-C<sub>4</sub>)alkyl, hydroxyl, (C<sub>1</sub>-C<sub>4</sub>)alkoxy, carboxyl, CONH<sub>2</sub>, -S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl, carboxylate (C<sub>1</sub>-C<sub>4</sub>)alkyl ester, or 1H-tetrazol-5-yl; or

when there are two  $X^6$  groups on one atom and both  $X^6$  are independently  $(C_1-C_6)$ alkyl, the two  $(C_1-C_6)$ alkyl groups may be optionally joined and, together with the atom to which the two  $X^6$  groups are attached, form a 4- to 9- membered ring optionally having oxygen, sulfur or  $NX^7$ ;

$X^7$  is hydrogen or  $(C_1-C_6)$ alkyl optionally substituted with hydroxyl; and

m for each occurrence is independently 0, 1 or 2;

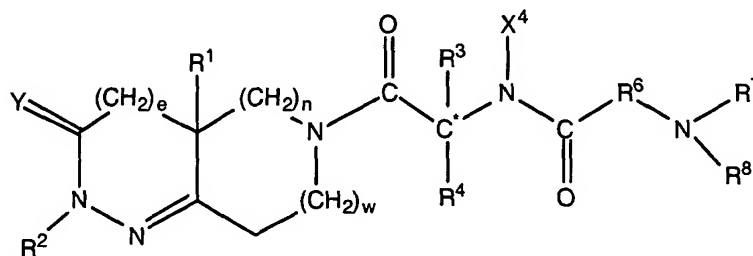
with the proviso that:

$X^6$  and  $X^{12}$  cannot be hydrogen when it is attached to C(O) or  $SO_2$  in the form  $C(O)X^6$ ,  $C(O)X^{12}$ ,  $SO_2X^6$  or  $SO_2X^{12}$ ; and

when  $R^6$  is a bond then L is  $N(X^2)$  and each r in the definition  $-(CH_2)_r-L-(CH_2)_r-$  is independently 2 or 3; wherein the method according to claim 1 which additionally comprises administering to a mammal in need thereof a growth hormone releasing hormone or a functional analog thereof.

8. (canceled)

9. (original) A method for increasing levels of endogenous growth hormone, which comprises administering to a human or other animal in need thereof effective amounts of a functional somatostatin antagonist and a compound of formula I



I

or the stereoisomeric mixtures, diastereomerically enriched, diastereomerically pure, enantiomerically enriched or enantiomerically pure isomers or the pharmaceutically acceptable salts and prodrugs thereof,

wherein

e is 0 or 1;

n and w are each independently 0, 1 or 2;

provided that w and n cannot both be 0 at the same time;

Y is oxygen or sulfur;

R<sup>1</sup> is hydrogen, -CN,  $-(CH_2)_qN(X^6)C(O)X^6$ ,  $-(CH_2)_qN(X^6)C(O)(CH_2)_rA^1$ ,

$-(CH_2)_qN(X^6)SO_2(CH_2)_rA^1$ ,  $-(CH_2)_qN(X^6)SO_2X^6$ ,  $-(CH_2)_qN(X^6)C(O)N(X^6)(CH_2)_rA^1$ ,

$-(CH_2)_qN(X^6)C(O)N(X^6)(X^6)$ ,  $-(CH_2)_qC(O)N(X^6)(X^6)$ ,  $-(CH_2)_qC(O)N(X^6)(CH_2)_tA^1$ ,  
 $-(CH_2)_qC(O)OX^6$ ,  $-(CH_2)_qC(O)O(CH_2)_tA^1$ ,  $-(CH_2)_qOX^6$ ,  $-(CH_2)_qOC(O)X^6$ ,  
 $-(CH_2)_qOC(O)(CH_2)_tA^1$ ,  $-(CH_2)_qOC(O)N(X^6)(CH_2)_tA^1$ ,  $-(CH_2)_qOC(O)N(X^6)(X^6)$ ,  
 $-(CH_2)_qC(O)X^6$ ,  $-(CH_2)_qC(O)(CH_2)_tA^1$ ,  $-(CH_2)_qN(X^6)C(O)OX^6$ ,  
 $-(CH_2)_qN(X^6)SO_2N(X^6)(X^6)$ ,  $-(CH_2)_qS(O)_mX^6$ ,  $-(CH_2)_qS(O)_m(CH_2)_tA^1$ ,  
 $-(C_1-C_{10})alkyl$ ,  $-(CH_2)_tA^1$ ,  $-(CH_2)_q-(C_3-C_7)cycloalkyl$ ,  $-(CH_2)_q-Y^1-(C_1-C_6)alkyl$ ,  
 $-(CH_2)_q-Y^1-(CH_2)_tA^1$  or  $-(CH_2)_q-Y^1-(CH_2)_t-(C_3-C_7)cycloalkyl$ ;

where the alkyl and cycloalkyl groups in the definition of  $R^1$  are optionally substituted with  $(C_1-C_4)alkyl$ , hydroxyl,  $(C_1-C_4)alkoxy$ , carboxyl,  $-CONH_2$ ,

$-S(O)_m(C_1-C_6)alkyl$ ,  $-CO_2(C_1-C_4)alkyl$  ester, 1H-tetrazol-5-yl or 1, 2 or 3 fluoro;

$Y^1$  is O,  $S(O)_m$ ,  $-C(O)NX^6$ -,  $-CH=CH-$ ,  $-C\equiv C-$ ,  $-N(X^6)C(O)-$ ,  $-C(O)NX^6$ -,

$-C(O)O-$ ,  $-OC(O)N(X^6)-$  or  $-OC(O)-$ ;

$q$  is 0, 1, 2, 3 or 4;

$t$  is 0, 1, 2 or 3;

said  $(CH_2)_q$  group and  $(CH_2)_t$  group may each be optionally substituted with hydroxyl,  $(C_1-C_4)alkoxy$ , carboxyl,  $-CONH_2$ ,  $-S(O)_m(C_1-C_6)alkyl$ ,

$-CO_2(C_1-C_4)alkyl$  ester, 1H-tetrazol-5-yl, 1, 2 or 3 fluoro, or 1 or 2  $(C_1-C_4)alkyl$ ;

$R^2$  is hydrogen,  $(C_1-C_6)alkyl$ ,  $-(C_0-C_3)alkyl-(C_3-C_6)cycloalkyl$ ,  $-(C_1-C_4)alkyl-A^1$  or  $A^1$ ;

where the alkyl groups and the cycloalkyl groups in the definition of  $R^2$  are optionally substituted with hydroxyl,  $-C(O)OX^6$ ,  $-C(O)N(X^6)(X^6)$ ,  $-N(X^6)(X^6)$ ,

$-S(O)_m(C_1-C_6)alkyl$ ,  $-C(O)A^1$ ,  $-C(O)(X^6)$ ,  $CF_3$ , CN or 1, 2 or 3 halogen;

$R^3$  is  $A^1$ ,  $(C_1-C_{10})alkyl$ ,  $-(C_1-C_6)alkyl-A^1$ ,  $-(C_1-C_6)alkyl-(C_3-C_7)cycloalkyl$ ,

$-(C_1-C_5)alkyl-X^1-(C_1-C_5)alkyl$ ,  $-(C_1-C_5)alkyl-X^1-(C_0-C_5)alkyl-A^1$  or

$-(C_1-C_5)alkyl-X^1-(C_1-C_5)alkyl-(C_3-C_7)cycloalkyl$ ;

where the alkyl groups in the definition of  $R^3$  are optionally substituted with

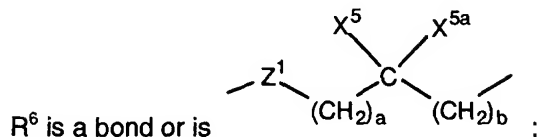
$-S(O)_m(C_1-C_6)alkyl$ ,  $-C(O)OX^3$ , 1, 2, 3, 4 or 5 halogens, or 1, 2 or 3  $OX^3$ ;

$X^1$  is O,  $S(O)_m$ ,  $-N(X^2)C(O)-$ ,  $-C(O)N(X^2)-$ ,  $-OC(O)-$ ,  $-C(O)O-$ ,  $-CX^2=CX^2-$ ,

$-N(X^2)C(O)O-$ ,  $-OC(O)N(X^2)-$  or  $-C\equiv C-$ ;

$R^4$  is hydrogen,  $(C_1-C_6)alkyl$  or  $(C_3-C_7)cycloalkyl$ , or  $R^4$  is taken together with  $R^3$  and the carbon atom to which they are attached and form  $(C_5-C_7)cycloalkyl$ ,  $(C_5-C_7)cycloalkenyl$ , a partially saturated or fully saturated 4- to 8-membered ring having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur and nitrogen, or is a bicyclic ring system consisting of a partially saturated or fully saturated 5- or 6-membered ring, fused to a partially saturated, fully unsaturated or fully saturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur and oxygen;

X<sup>4</sup> is hydrogen or (C<sub>1</sub>-C<sub>6</sub>)alkyl or X<sup>4</sup> is taken together with R<sup>4</sup> and the nitrogen atom to which X<sup>4</sup> is attached and the carbon atom to which R<sup>4</sup> is attached and form a five to seven membered ring;



where a and b are independently 0, 1, 2 or 3;

X<sup>5</sup> and X<sup>5a</sup> are each independently selected from the group consisting of hydrogen, trifluoromethyl, A<sup>1</sup> and optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl;

the optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl in the definition of X<sup>5</sup> and X<sup>5a</sup> is optionally substituted with a substituent selected from the group consisting of A<sup>1</sup>, OX<sup>2</sup>, -S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl, -C(O)OX<sup>2</sup>, (C<sub>3</sub>-C<sub>7</sub>)cycloalkyl, -N(X<sup>2</sup>)(X<sup>2</sup>) and -C(O)N(X<sup>2</sup>)(X<sup>2</sup>);

or the carbon bearing X<sup>5</sup> or X<sup>5a</sup> forms one or two alkylene bridges with the nitrogen atom bearing R<sup>7</sup> and R<sup>8</sup> wherein each alkylene bridge contains 1 to 5 carbon atoms, provided that when one alkylene bridge is formed then X<sup>5</sup> or X<sup>5a</sup> but not both may be on the carbon atom and R<sup>7</sup> or R<sup>8</sup> but not both may be on the nitrogen atom and further provided that when two alkylene bridges are formed then X<sup>5</sup> and X<sup>5a</sup> cannot be on the carbon atom and R<sup>7</sup> and R<sup>8</sup> cannot be on the nitrogen atom;

or X<sup>5</sup> is taken together with X<sup>5a</sup> and the carbon atom to which they are attached and form a partially saturated or fully saturated 3- to 7-membered ring, or a partially saturated or fully saturated 4- to 8-membered ring having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur and nitrogen;

or X<sup>5</sup> is taken together with X<sup>5a</sup> and the carbon atom to which they are attached and form a bicyclic ring system consisting of a partially saturated or fully saturated 5- or 6-membered ring, optionally having 1 or 2 heteroatoms independently selected from the group consisting of nitrogen, sulfur and oxygen, fused to a partially saturated, fully saturated or fully unsaturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur and oxygen;

Z<sup>1</sup> is a bond, O or N-X<sup>2</sup>, provided that when a and b are both 0 then Z<sup>1</sup> is not N-X<sup>2</sup> or O;

R<sup>7</sup> and R<sup>8</sup> are independently hydrogen or optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl;

where the optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl in the definition of R<sup>7</sup> and R<sup>8</sup> is optionally independently substituted with A<sup>1</sup>, -C(O)O-(C<sub>1</sub>-C<sub>6</sub>)alkyl,

$-\text{S}(\text{O})_m(\text{C}_1-\text{C}_6)\text{alkyl}$ , 1 to 5 halogens, 1 to 3 hydroxy, 1 to 3  $-\text{O}-\text{C}(\text{O})(\text{C}_1-\text{C}_{10})\text{alkyl}$  or 1 to 3  $(\text{C}_1-\text{C}_6)\text{alkoxy}$ ; or

$\text{R}^7$  and  $\text{R}^8$  can be taken together to form  $-(\text{CH}_2)_r-\text{L}-(\text{CH}_2)_r-$ ;

where L is  $\text{C}(\text{X}^2)(\text{X}^2)$ ,  $\text{S}(\text{O})_m$  or  $\text{N}(\text{X}^2)$ ;

$\text{A}^1$  for each occurrence is independently  $(\text{C}_5-\text{C}_7)\text{cycloalkenyl}$ , phenyl or a partially saturated, fully saturated or fully unsaturated 4- to 8-membered ring optionally having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur and nitrogen, a bicyclic ring system consisting of a partially saturated, fully unsaturated or fully saturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur and oxygen, fused to a partially saturated, fully saturated or fully unsaturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur and oxygen;

$\text{A}^1$  for each occurrence is independently optionally substituted, in one or optionally both rings if  $\text{A}^1$  is a bicyclic ring system, with up to three substituents, each substituent independently selected from the group consisting of F, Cl, Br, I,  $\text{OCF}_3$ ,  $\text{OCF}_2\text{H}$ ,  $\text{CF}_3$ ,  $\text{CH}_3$ ,  $\text{OCH}_3$ ,  $-\text{OX}^6$ ,  $-\text{C}(\text{O})\text{N}(\text{X}^6)(\text{X}^6)$ ,  $-\text{C}(\text{O})\text{OX}^6$ , oxo,  $(\text{C}_1-\text{C}_6)\text{alkyl}$ , nitro, cyano, benzyl,  $-\text{S}(\text{O})_m(\text{C}_1-\text{C}_6)\text{alkyl}$ , 1H-tetrazol-5-yl, phenyl, phenoxy, phenylalkyloxy, halophenyl, methylenedioxy,  $-\text{N}(\text{X}^6)(\text{X}^6)$ ,  $-\text{N}(\text{X}^6)\text{C}(\text{O})(\text{X}^6)$ ,  $-\text{SO}_2\text{N}(\text{X}^6)(\text{X}^6)$ ,  $-\text{N}(\text{X}^6)\text{SO}_2\text{-phenyl}$ ,  $-\text{N}(\text{X}^6)\text{SO}_2\text{X}^6$ ,  $-\text{CONX}^{11}\text{X}^{12}$ ,  $-\text{SO}_2\text{NX}^{11}\text{X}^{12}$ ,  $-\text{NX}^6\text{SO}_2\text{X}^{12}$ ,  $-\text{NX}^6\text{CONX}^{11}\text{X}^{12}$ ,  $-\text{NX}^6\text{SO}_2\text{NX}^{11}\text{X}^{12}$ ,  $-\text{NX}^6\text{C}(\text{O})\text{X}^{12}$ , imidazolyl, thiazolyl and tetrazolyl, provided that if  $\text{A}^1$  is optionally substituted with methylenedioxy then it can only be substituted with one methylenedioxy;

where  $\text{X}^{11}$  is hydrogen or optionally substituted  $(\text{C}_1-\text{C}_6)\text{alkyl}$ ;

the optionally substituted  $(\text{C}_1-\text{C}_6)\text{alkyl}$  defined for  $\text{X}^{11}$  is optionally independently substituted with phenyl, phenoxy,  $(\text{C}_1-\text{C}_6)\text{alkoxycarbonyl}$ ,  $-\text{S}(\text{O})_m(\text{C}_1-\text{C}_6)\text{alkyl}$ , 1 to 5 halogens, 1 to 3 hydroxy, 1 to 3  $(\text{C}_1-\text{C}_{10})\text{alkanoyloxy}$  or 1 to 3  $(\text{C}_1-\text{C}_6)\text{alkoxy}$ ;

$\text{X}^{12}$  is hydrogen,  $(\text{C}_1-\text{C}_6)\text{alkyl}$ , phenyl, thiazolyl, imidazolyl, furyl or thienyl, provided that when  $\text{X}^{12}$  is not hydrogen,  $\text{X}^{12}$  is optionally substituted with one to three substituents independently selected from the group consisting of Cl, F,  $\text{CH}_3$ ,  $\text{OCH}_3$ ,  $\text{OCF}_3$  and  $\text{CF}_3$ ;

or  $\text{X}^{11}$  and  $\text{X}^{12}$  are taken together to form  $-(\text{CH}_2)_r-\text{L}^1-(\text{CH}_2)_r-$ ;

where  $\text{L}^1$  is  $\text{C}(\text{X}^2)(\text{X}^2)$ , O,  $\text{S}(\text{O})_m$  or  $\text{N}(\text{X}^2)$ ;

r for each occurrence is independently 1, 2 or 3;

$X^2$  for each occurrence is independently hydrogen, optionally substituted  $(C_1-C_6)$ alkyl, or optionally substituted  $(C_3-C_7)$ cycloalkyl, where the optionally substituted  $(C_1-C_6)$ alkyl and optionally substituted  $(C_3-C_7)$ cycloalkyl in the definition of  $X^2$  are optionally independently substituted with  $-S(O)_m(C_1-C_6)$ alkyl,  $-C(O)OX^3$ , 1 to 5 halogens or 1-3  $OX^3$ ;

$X^3$  for each occurrence is independently hydrogen or  $(C_1-C_6)$ alkyl;

$X^6$  is independently hydrogen, optionally substituted  $(C_1-C_6)$ alkyl,  $(C_2-C_6)$ halogenated alkyl, optionally substituted  $(C_3-C_7)$ cycloalkyl,  $(C_3-C_7)$ -halogenatedcycloalkyl, where optionally substituted  $(C_1-C_6)$ alkyl and optionally substituted  $(C_3-C_7)$ cycloalkyl in the definition of  $X^6$  is optionally independently substituted by 1 or 2  $(C_1-C_4)$ alkyl, hydroxyl,  $(C_1-C_4)$ alkoxy, carboxyl,  $CONH_2$ ,  $-S(O)_m(C_1-C_6)$ alkyl, carboxylate  $(C_1-C_4)$ alkyl ester, or 1H-tetrazol-5-yl; or

when there are two  $X^6$  groups on one atom and both  $X^6$  are independently  $(C_1-C_6)$ alkyl, the two  $(C_1-C_6)$ alkyl groups may be optionally joined and, together with the atom to which the two  $X^6$  groups are attached, form a 4- to 9- membered ring optionally having oxygen, sulfur or  $NX^7$ ;

$X^7$  is hydrogen or  $(C_1-C_6)$ alkyl optionally substituted with hydroxyl; and

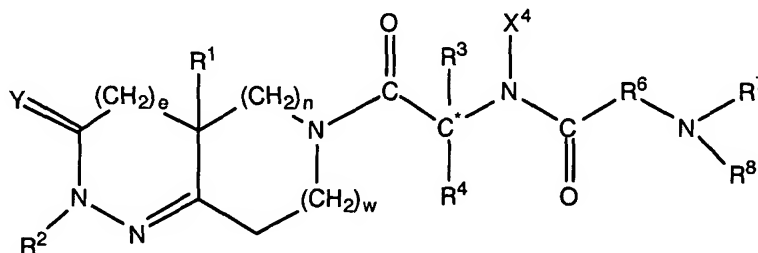
$m$  for each occurrence is independently 0, 1 or 2;

with the proviso that:

$X^6$  and  $X^{12}$  cannot be hydrogen when it is attached to  $C(O)$  or  $SO_2$  in the form  $C(O)X^6$ ,  $C(O)X^{12}$ ,  $SO_2X^6$  or  $SO_2X^{12}$ ; and

when  $R^6$  is a bond then  $L$  is  $N(X^2)$  and each  $r$  in the definition  $-(CH_2)_r-L-(CH_2)_r-$  is independently 2 or 3.

10. (original) A method of treating or preventing congestive heart failure, obesity or frailty associated with aging, which comprises administering to a mammal in need thereof effective amounts of a functional somatostatin antagonist and a compound of formula I



I

or the stereoisomeric mixtures, diastereomerically enriched, diastereomerically pure, enantiomerically enriched or enantiomerically pure isomers or the pharmaceutically acceptable salts and prodrugs thereof,

wherein

e is 0 or 1;

n and w are each independently 0, 1 or 2;

provided that w and n cannot both be 0 at the same time;

Y is oxygen or sulfur;

R<sup>1</sup> is hydrogen, -CN, -(CH<sub>2</sub>)<sub>q</sub>N(X<sup>6</sup>)C(O)X<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>N(X<sup>6</sup>)C(O)(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>,  
-(CH<sub>2</sub>)<sub>q</sub>N(X<sup>6</sup>)SO<sub>2</sub>(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>N(X<sup>6</sup>)SO<sub>2</sub>X<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>N(X<sup>6</sup>)C(O)N(X<sup>6</sup>)(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>,  
-(CH<sub>2</sub>)<sub>q</sub>N(X<sup>6</sup>)C(O)N(X<sup>6</sup>)(X<sup>6</sup>), -(CH<sub>2</sub>)<sub>q</sub>C(O)N(X<sup>6</sup>)(X<sup>6</sup>), -(CH<sub>2</sub>)<sub>q</sub>C(O)N(X<sup>6</sup>)(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>,  
-(CH<sub>2</sub>)<sub>q</sub>C(O)OX<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>C(O)O(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>OX<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>OC(O)X<sup>6</sup>,  
-(CH<sub>2</sub>)<sub>q</sub>OC(O)(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>OC(O)N(X<sup>6</sup>)(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>OC(O)N(X<sup>6</sup>)(X<sup>6</sup>),  
-(CH<sub>2</sub>)<sub>q</sub>C(O)X<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>C(O)(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>N(X<sup>6</sup>)C(O)OX<sup>6</sup>,  
-(CH<sub>2</sub>)<sub>q</sub>N(X<sup>6</sup>)SO<sub>2</sub>N(X<sup>6</sup>)(X<sup>6</sup>), -(CH<sub>2</sub>)<sub>q</sub>S(O)<sub>m</sub>X<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>S(O)<sub>m</sub>(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>,  
-(C<sub>1</sub>-C<sub>10</sub>)alkyl, -(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>-(C<sub>3</sub>-C<sub>7</sub>)cycloalkyl, -(CH<sub>2</sub>)<sub>q</sub>-Y<sup>1</sup>-(C<sub>1</sub>-C<sub>6</sub>)alkyl,  
-(CH<sub>2</sub>)<sub>q</sub>-Y<sup>1</sup>-(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup> or -(CH<sub>2</sub>)<sub>q</sub>-Y<sup>1</sup>-(CH<sub>2</sub>)<sub>t</sub>-(C<sub>3</sub>-C<sub>7</sub>)cycloalkyl;

where the alkyl and cycloalkyl groups in the definition of R<sup>1</sup> are optionally substituted  
with (C<sub>1</sub>-C<sub>4</sub>)alkyl, hydroxyl, (C<sub>1</sub>-C<sub>4</sub>)alkoxy, carboxyl, -CONH<sub>2</sub>,

-S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl, -CO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub>)alkyl ester, 1H-tetrazol-5-yl or 1, 2 or 3 fluoro;

Y<sup>1</sup> is O, S(O)<sub>m</sub>, -C(O)NX<sup>6</sup>-, -CH=CH-, -C≡C-, -N(X<sup>6</sup>)C(O)-, -C(O)NX<sup>6</sup>-,

-C(O)O-, -OC(O)N(X<sup>6</sup>)- or -OC(O)-;

q is 0, 1, 2, 3 or 4;

t is 0, 1, 2 or 3;

said (CH<sub>2</sub>)<sub>q</sub> group and (CH<sub>2</sub>)<sub>t</sub> group may each be optionally substituted with hydroxyl,

(C<sub>1</sub>-C<sub>4</sub>)alkoxy, carboxyl, -CONH<sub>2</sub>, -S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl,

-CO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub>)alkyl ester, 1H-tetrazol-5-yl, 1, 2 or 3 fluoro, or 1 or 2 (C<sub>1</sub>-C<sub>4</sub>)alkyl;

R<sup>2</sup> is hydrogen, (C<sub>1</sub>-C<sub>8</sub>)alkyl, -(C<sub>0</sub>-C<sub>3</sub>)alkyl-(C<sub>3</sub>-C<sub>8</sub>)cycloalkyl, -(C<sub>1</sub>-C<sub>4</sub>)alkyl-A<sup>1</sup> or A<sup>1</sup>;

where the alkyl groups and the cycloalkyl groups in the definition of R<sup>2</sup> are optionally  
substituted with hydroxyl, -C(O)OX<sup>6</sup>, -C(O)N(X<sup>6</sup>)(X<sup>6</sup>), -N(X<sup>6</sup>)(X<sup>6</sup>),

-S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl, -C(O)A<sup>1</sup>, -C(O)(X<sup>6</sup>), CF<sub>3</sub>, CN or 1, 2 or 3 halogen;

R<sup>3</sup> is A<sup>1</sup>, (C<sub>1</sub>-C<sub>10</sub>)alkyl, -(C<sub>1</sub>-C<sub>6</sub>)alkyl-A<sup>1</sup>, -(C<sub>1</sub>-C<sub>6</sub>)alkyl-(C<sub>3</sub>-C<sub>7</sub>)cycloalkyl,

-(C<sub>1</sub>-C<sub>5</sub>)alkyl-X<sup>1</sup>-(C<sub>1</sub>-C<sub>5</sub>)alkyl, -(C<sub>1</sub>-C<sub>5</sub>)alkyl-X<sup>1</sup>-(C<sub>0</sub>-C<sub>5</sub>)alkyl-A<sup>1</sup> or

-(C<sub>1</sub>-C<sub>5</sub>)alkyl-X<sup>1</sup>-(C<sub>1</sub>-C<sub>5</sub>)alkyl-(C<sub>3</sub>-C<sub>7</sub>)cycloalkyl;

where the alkyl groups in the definition of R<sup>3</sup> are optionally substituted with

-S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl, -C(O)OX<sup>3</sup>, 1, 2, 3, 4 or 5 halogens, or 1, 2 or 3 OX<sup>3</sup>;

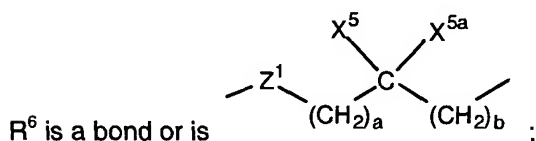
X<sup>1</sup> is O, S(O)<sub>m</sub>, -N(X<sup>2</sup>)C(O)-, -C(O)N(X<sup>2</sup>)-, -OC(O)-, -C(O)O-, -CX<sup>2</sup>=CX<sup>2</sup>-,

-N(X<sup>2</sup>)C(O)O-, -OC(O)N(X<sup>2</sup>)- or -C≡C-;

R<sup>4</sup> is hydrogen, (C<sub>1</sub>-C<sub>6</sub>)alkyl or (C<sub>3</sub>-C<sub>7</sub>)cycloalkyl, or R<sup>4</sup> is taken together with R<sup>3</sup> and the  
carbon atom to which they are attached and form (C<sub>5</sub>-C<sub>7</sub>)cycloalkyl, (C<sub>5</sub>-C<sub>7</sub>)cycloalkenyl, a

partially saturated or fully saturated 4- to 8-membered ring having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur and nitrogen, or is a bicyclic ring system consisting of a partially saturated or fully saturated 5- or 6-membered ring, fused to a partially saturated, fully unsaturated or fully saturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur and oxygen;

$X^4$  is hydrogen or  $(C_1-C_6)$ alkyl or  $X^4$  is taken together with  $R^4$  and the nitrogen atom to which  $X^4$  is attached and the carbon atom to which  $R^4$  is attached and form a five to seven membered ring;



where a and b are independently 0, 1, 2 or 3;

$X^5$  and  $X^{5a}$  are each independently selected from the group consisting of hydrogen, trifluoromethyl,  $A^1$  and optionally substituted  $(C_1-C_6)$ alkyl;

the optionally substituted  $(C_1-C_6)$ alkyl in the definition of  $X^5$  and  $X^{5a}$  is optionally substituted with a substituent selected from the group consisting of  $A^1$ ,  $OX^2$ ,  $-S(O)_m(C_1-C_6)$ alkyl,  $-C(O)OX^2$ ,  $(C_3-C_7)$ cycloalkyl,  $-N(X^2)(X^2)$  and  $-C(O)N(X^2)(X^2)$ ;

or the carbon bearing  $X^5$  or  $X^{5a}$  forms one or two alkylene bridges with the nitrogen atom bearing  $R^7$  and  $R^8$  wherein each alkylene bridge contains 1 to 5 carbon atoms, provided that when one alkylene bridge is formed then  $X^5$  or  $X^{5a}$  but not both may be on the carbon atom and  $R^7$  or  $R^8$  but not both may be on the nitrogen atom and further provided that when two alkylene bridges are formed then  $X^5$  and  $X^{5a}$  cannot be on the carbon atom and  $R^7$  and  $R^8$  cannot be on the nitrogen atom;

or  $X^5$  is taken together with  $X^{5a}$  and the carbon atom to which they are attached and form a partially saturated or fully saturated 3- to 7-membered ring, or a partially saturated or fully saturated 4- to 8-membered ring having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur and nitrogen;

or  $X^5$  is taken together with  $X^{5a}$  and the carbon atom to which they are attached and form a bicyclic ring system consisting of a partially saturated or fully saturated 5- or 6-membered ring, optionally having 1 or 2 heteroatoms independently selected from the group consisting of nitrogen, sulfur and oxygen, fused to a partially saturated, fully saturated or fully unsaturated 5- or 6-membered ring, optionally having 1 to 4

heteroatoms independently selected from the group consisting of nitrogen, sulfur and oxygen;

Z<sup>1</sup> is a bond, O or N-X<sup>2</sup>, provided that when a and b are both 0 then Z<sup>1</sup> is not N-X<sup>2</sup> or O;

R<sup>7</sup> and R<sup>8</sup> are independently hydrogen or optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl;

where the optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl in the definition of R<sup>7</sup> and R<sup>8</sup> is optionally independently substituted with A<sup>1</sup>, -C(O)O-(C<sub>1</sub>-C<sub>6</sub>)alkyl,

-S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl, 1 to 5 halogens, 1 to 3 hydroxy, 1 to 3 -O-C(O)(C<sub>1</sub>-C<sub>10</sub>)alkyl or 1 to 3 (C<sub>1</sub>-C<sub>6</sub>)alkoxy; or

R<sup>7</sup> and R<sup>8</sup> can be taken together to form -(CH<sub>2</sub>)<sub>r</sub>-L-(CH<sub>2</sub>)<sub>r</sub>;

where L is C(X<sup>2</sup>)(X<sup>2</sup>), S(O)<sub>m</sub> or N(X<sup>2</sup>);

A<sup>1</sup> for each occurrence is independently (C<sub>5</sub>-C<sub>7</sub>)cycloalkenyl, phenyl or a partially saturated, fully saturated or fully unsaturated 4- to 8-membered ring optionally having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur and nitrogen, a bicyclic ring system consisting of a partially saturated, fully unsaturated or fully saturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur and oxygen, fused to a partially saturated, fully saturated or fully unsaturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur and oxygen;

A<sup>1</sup> for each occurrence is independently optionally substituted, in one or optionally both rings if A<sup>1</sup> is a bicyclic ring system, with up to three substituents, each substituent independently selected from the group consisting of F, Cl, Br, I, OCF<sub>3</sub>, OCF<sub>2</sub>H, CF<sub>3</sub>, CH<sub>3</sub>, OCH<sub>3</sub>, -OX<sup>6</sup>,

-C(O)N(X<sup>6</sup>)(X<sup>6</sup>), -C(O)OX<sup>6</sup>, oxo, (C<sub>1</sub>-C<sub>6</sub>)alkyl, nitro, cyano, benzyl,

-S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl, 1H-tetrazol-5-yl, phenyl, phenoxy, phenylalkyloxy, halophenyl, methylenedioxy, -N(X<sup>6</sup>)(X<sup>6</sup>), -N(X<sup>6</sup>)C(O)(X<sup>6</sup>), -SO<sub>2</sub>N(X<sup>6</sup>)(X<sup>6</sup>),

-N(X<sup>6</sup>)SO<sub>2</sub>-phenyl, -N(X<sup>6</sup>)SO<sub>2</sub>X<sup>6</sup>, -CONX<sup>11</sup>X<sup>12</sup>, -SO<sub>2</sub>NX<sup>11</sup>X<sup>12</sup>, -NX<sup>6</sup>SO<sub>2</sub>X<sup>12</sup>,

-NX<sup>6</sup>CONX<sup>11</sup>X<sup>12</sup>, -NX<sup>6</sup>SO<sub>2</sub>NX<sup>11</sup>X<sup>12</sup>, -NX<sup>6</sup>C(O)X<sup>12</sup>, imidazolyl, thiazolyl and tetrazolyl,

provided that if A<sup>1</sup> is optionally substituted with methylenedioxy then it can only be substituted with one methylenedioxy;

where X<sup>11</sup> is hydrogen or optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl;

the optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl defined for X<sup>11</sup> is optionally independently substituted with phenyl, phenoxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, -S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl, 1 to 5 halogens, 1 to 3 hydroxy, 1 to 3 (C<sub>1</sub>-C<sub>10</sub>)alkanoyloxy or 1 to 3 (C<sub>1</sub>-C<sub>6</sub>)alkoxy;

$X^{12}$  is hydrogen, (C<sub>1</sub>-C<sub>6</sub>)alkyl, phenyl, thiazolyl, imidazolyl, furyl or thienyl, provided that when  $X^{12}$  is not hydrogen,  $X^{12}$  is optionally substituted with one to three substituents independently selected from the group consisting of Cl, F, CH<sub>3</sub>, OCH<sub>3</sub>, OCF<sub>3</sub> and CF<sub>3</sub>;

or  $X^{11}$  and  $X^{12}$  are taken together to form  $-(CH_2)_r-L^1-(CH_2)_r-$ ;

where  $L^1$  is  $C(X^2)(X^2)$ , O, S(O)<sub>m</sub> or N( $X^2$ );

r for each occurrence is independently 1, 2 or 3;

$X^2$  for each occurrence is independently hydrogen, optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl, or optionally substituted (C<sub>3</sub>-C<sub>7</sub>)cycloalkyl, where the optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl and optionally substituted (C<sub>3</sub>-C<sub>7</sub>)cycloalkyl in the definition of  $X^2$  are optionally independently substituted with -S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl, -C(O)OX<sup>3</sup>, 1 to 5 halogens or 1-3 OX<sup>3</sup>;

$X^3$  for each occurrence is independently hydrogen or (C<sub>1</sub>-C<sub>6</sub>)alkyl;

$X^6$  is independently hydrogen, optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>2</sub>-C<sub>6</sub>)halogenated alkyl, optionally substituted (C<sub>3</sub>-C<sub>7</sub>)cycloalkyl, (C<sub>3</sub>-C<sub>7</sub>)-halogenatedcycloalkyl, where optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl and optionally substituted (C<sub>3</sub>-C<sub>7</sub>)cycloalkyl in the definition of  $X^6$  is optionally independently substituted by 1 or 2 (C<sub>1</sub>-C<sub>4</sub>)alkyl, hydroxyl, (C<sub>1</sub>-C<sub>4</sub>)alkoxy, carboxyl, CONH<sub>2</sub>, -S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl, carboxylate (C<sub>1</sub>-C<sub>4</sub>)alkyl ester, or 1H-tetrazol-5-yl; or

when there are two  $X^6$  groups on one atom and both  $X^6$  are independently (C<sub>1</sub>-C<sub>6</sub>)alkyl, the two (C<sub>1</sub>-C<sub>6</sub>)alkyl groups may be optionally joined and, together with the atom to which the two  $X^6$  groups are attached, form a 4- to 9- membered ring optionally having oxygen, sulfur or NX<sup>7</sup>;

$X^7$  is hydrogen or (C<sub>1</sub>-C<sub>6</sub>)alkyl optionally substituted with hydroxyl; and

m for each occurrence is independently 0, 1 or 2;

with the proviso that:

$X^6$  and  $X^{12}$  cannot be hydrogen when it is attached to C(O) or SO<sub>2</sub> in the form C(O)X<sup>6</sup>, C(O)X<sup>12</sup>, SO<sub>2</sub>X<sup>6</sup> or SO<sub>2</sub>X<sup>12</sup>; and

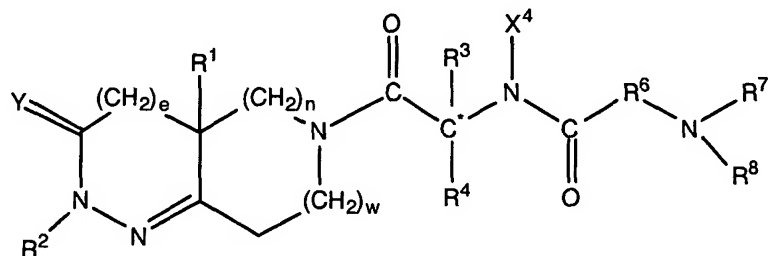
when R<sup>6</sup> is a bond then L is N( $X^2$ ) and each r in the definition  $-(CH_2)_r-L-(CH_2)_r-$  is independently 2 or 3.

11. (original) A method according to claim 10 wherein said functional somatostatin antagonist is an alpha-2 adrenergic agonist.

12. (original) A method according to claim 11 wherein said alpha-2 adrenergic agonist is selected from the group consisting of clonidine, xylazine and medetomidine.

13. (original) A method according to claim 12 wherein said compound of formula I is 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide L-tartaric acid salt.

14. (original) A pharmaceutical composition which comprises a pharmaceutically acceptable carrier, an amount of an alpha-2 adrenergic agonist and an amount of a compound of formula I



I

or the stereoisomeric mixtures, diastereomerically enriched, diastereomerically pure, enantiomerically enriched or enantiomerically pure isomers or the pharmaceutically acceptable salts and prodrugs thereof,

wherein

e is 0 or 1;

n and w are each independently 0, 1 or 2;

provided that w and n cannot both be 0 at the same time;

Y is oxygen or sulfur;

R<sup>1</sup> is hydrogen, -CN, -(CH<sub>2</sub>)<sub>q</sub>N(X<sup>6</sup>)C(O)X<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>N(X<sup>6</sup>)C(O)(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>N(X<sup>6</sup>)SO<sub>2</sub>(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>N(X<sup>6</sup>)SO<sub>2</sub>X<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>N(X<sup>6</sup>)C(O)N(X<sup>6</sup>)(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>N(X<sup>6</sup>)C(O)N(X<sup>6</sup>)(X<sup>6</sup>), -(CH<sub>2</sub>)<sub>q</sub>C(O)N(X<sup>6</sup>)(X<sup>6</sup>), -(CH<sub>2</sub>)<sub>q</sub>C(O)N(X<sup>6</sup>)(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>C(O)OX<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>C(O)O(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>OX<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>OC(O)X<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>OC(O)(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>OC(O)N(X<sup>6</sup>)(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>OC(O)N(X<sup>6</sup>)(X<sup>6</sup>), -(CH<sub>2</sub>)<sub>q</sub>C(O)X<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>C(O)(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>N(X<sup>6</sup>)C(O)OX<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>N(X<sup>6</sup>)SO<sub>2</sub>N(X<sup>6</sup>)(X<sup>6</sup>), -(CH<sub>2</sub>)<sub>q</sub>S(O)<sub>m</sub>X<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>S(O)<sub>m</sub>(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(C<sub>1</sub>-C<sub>10</sub>)alkyl, -(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>-(C<sub>3</sub>-C<sub>7</sub>)cycloalkyl, -(CH<sub>2</sub>)<sub>q</sub>-Y<sup>1</sup>-(C<sub>1</sub>-C<sub>6</sub>)alkyl, -(CH<sub>2</sub>)<sub>q</sub>-Y<sup>1</sup>-(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup> or -(CH<sub>2</sub>)<sub>q</sub>-Y<sup>1</sup>-(CH<sub>2</sub>)<sub>t</sub>-(C<sub>3</sub>-C<sub>7</sub>)cycloalkyl;

where the alkyl and cycloalkyl groups in the definition of R<sup>1</sup> are optionally substituted with (C<sub>1</sub>-C<sub>4</sub>)alkyl, hydroxyl, (C<sub>1</sub>-C<sub>4</sub>)alkoxy, carboxyl, -CONH<sub>2</sub>,

-S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl, -CO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub>)alkyl ester, 1H-tetrazol-5-yl or 1, 2 or 3 fluoro;

Y<sup>1</sup> is O, S(O)<sub>m</sub>, -C(O)NX<sup>6</sup>-, -CH=CH-, -C≡C-, -N(X<sup>6</sup>)C(O)-, -C(O)NX<sup>6</sup>-,

-C(O)O-, -OC(O)N(X<sup>6</sup>)- or -OC(O)-;

q is 0, 1, 2, 3 or 4;

t is 0, 1, 2 or 3;

said  $(CH_2)_q$  group and  $(CH_2)_t$  group may each be optionally substituted with hydroxyl,  $(C_1-C_4)$ alkoxy, carboxyl,  $-CONH_2$ ,  $-S(O)_m(C_1-C_6)$ alkyl,

$-CO_2(C_1-C_4)$ alkyl ester, 1H-tetrazol-5-yl, 1, 2 or 3 fluoro, or 1 or 2  $(C_1-C_4)$ alkyl;

$R^2$  is hydrogen,  $(C_1-C_8)$ alkyl,  $-(C_0-C_3)$ alkyl- $(C_3-C_8)$ cycloalkyl,  $-(C_1-C_4)$ alkyl- $A^1$  or  $A^1$ ;

where the alkyl groups and the cycloalkyl groups in the definition of  $R^2$  are optionally substituted with hydroxyl,  $-C(O)OX^6$ ,  $-C(O)N(X^6)(X^6)$ ,  $-N(X^6)(X^6)$ ,

$-S(O)_m(C_1-C_6)$ alkyl,  $-C(O)A^1$ ,  $-C(O)(X^6)$ ,  $CF_3$ ,  $CN$  or 1, 2 or 3 halogen;

$R^3$  is  $A^1$ ,  $(C_1-C_{10})$ alkyl,  $-(C_1-C_6)$ alkyl- $A^1$ ,  $-(C_1-C_6)$ alkyl- $(C_3-C_7)$ cycloalkyl,

$-(C_1-C_5)$ alkyl- $X^1$ -( $C_1-C_5$ )alkyl,  $-(C_1-C_5)$ alkyl- $X^1$ -( $C_0-C_5$ )alkyl- $A^1$  or

$-(C_1-C_5)$ alkyl- $X^1$ -( $C_1-C_5$ )alkyl- $(C_3-C_7)$ cycloalkyl;

where the alkyl groups in the definition of  $R^3$  are optionally substituted with

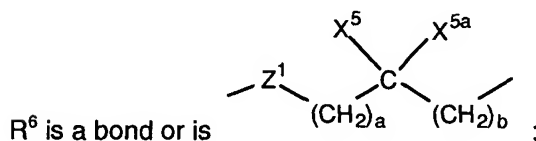
$-S(O)_m(C_1-C_6)$ alkyl,  $-C(O)OX^3$ , 1, 2, 3, 4 or 5 halogens, or 1, 2 or 3  $OX^3$ ;

$X^1$  is O,  $S(O)_m$ ,  $-N(X^2)C(O)-$ ,  $-C(O)N(X^2)-$ ,  $-OC(O)-$ ,  $-C(O)O-$ ,  $-CX^2=CX^2-$ ,

$-N(X^2)C(O)O-$ ,  $-OC(O)N(X^2)-$  or  $-C\equiv C-$ ;

$R^4$  is hydrogen,  $(C_1-C_6)$ alkyl or  $(C_3-C_7)$ cycloalkyl, or  $R^4$  is taken together with  $R^3$  and the carbon atom to which they are attached and form  $(C_5-C_7)$ cycloalkyl,  $(C_5-C_7)$ cycloalkenyl, a partially saturated or fully saturated 4- to 8-membered ring having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur and nitrogen, or is a bicyclic ring system consisting of a partially saturated or fully saturated 5- or 6-membered ring, fused to a partially saturated, fully unsaturated or fully saturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur and oxygen;

$X^4$  is hydrogen or  $(C_1-C_6)$ alkyl or  $X^4$  is taken together with  $R^4$  and the nitrogen atom to which  $X^4$  is attached and the carbon atom to which  $R^4$  is attached and form a five to seven membered ring;



where a and b are independently 0, 1, 2 or 3;

$X^5$  and  $X^{5a}$  are each independently selected from the group consisting of hydrogen, trifluoromethyl,  $A^1$  and optionally substituted  $(C_1-C_6)$ alkyl;

the optionally substituted  $(C_1-C_6)$ alkyl in the definition of  $X^5$  and  $X^{5a}$  is optionally substituted with a substituent selected from the group consisting of

$A^1$ ,  $OX^2$ ,  $-S(O)_m(C_1-C_6)alkyl$ ,  $-C(O)OX^2$ ,  $(C_3-C_7)cycloalkyl$ ,  $-N(X^2)(X^2)$  and  $-C(O)N(X^2)(X^2)$ ;

or the carbon bearing  $X^5$  or  $X^{5a}$  forms one or two alkylene bridges with the nitrogen atom bearing  $R^7$  and  $R^8$  wherein each alkylene bridge contains 1 to 5 carbon atoms, provided that when one alkylene bridge is formed then  $X^5$  or  $X^{5a}$  but not both may be on the carbon atom and  $R^7$  or  $R^8$  but not both may be on the nitrogen atom and further provided that when two alkylene bridges are formed then  $X^5$  and  $X^{5a}$  cannot be on the carbon atom and  $R^7$  and  $R^8$  cannot be on the nitrogen atom;

or  $X^5$  is taken together with  $X^{5a}$  and the carbon atom to which they are attached and form a partially saturated or fully saturated 3- to 7-membered ring, or a partially saturated or fully saturated 4- to 8-membered ring having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur and nitrogen;

or  $X^5$  is taken together with  $X^{5a}$  and the carbon atom to which they are attached and form a bicyclic ring system consisting of a partially saturated or fully saturated 5- or 6-membered ring, optionally having 1 or 2 heteroatoms independently selected from the group consisting of nitrogen, sulfur and oxygen, fused to a partially saturated, fully saturated or fully unsaturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur and oxygen;

$Z^1$  is a bond, O or  $N-X^2$ , provided that when a and b are both 0 then  $Z^1$  is not  $N-X^2$  or O;

$R^7$  and  $R^8$  are independently hydrogen or optionally substituted  $(C_1-C_6)alkyl$ ;

where the optionally substituted  $(C_1-C_6)alkyl$  in the definition of  $R^7$  and  $R^8$  is optionally independently substituted with  $A^1$ ,  $-C(O)O-(C_1-C_6)alkyl$ ,

$-S(O)_m(C_1-C_6)alkyl$ , 1 to 5 halogens, 1 to 3 hydroxy, 1 to 3  $-O-C(O)(C_1-C_{10})alkyl$  or 1 to 3  $(C_1-C_6)alkoxy$ ; or

$R^7$  and  $R^8$  can be taken together to form  $-(CH_2)_r-L-(CH_2)_r-$ ;

where L is  $C(X^2)(X^2)$ ,  $S(O)_m$  or  $N(X^2)$ ;

$A^1$  for each occurrence is independently  $(C_5-C_7)cycloalkenyl$ , phenyl or a partially saturated, fully saturated or fully unsaturated 4- to 8-membered ring optionally having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur and nitrogen, a bicyclic ring system consisting of a partially saturated, fully unsaturated or fully saturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur and oxygen, fused to a partially saturated, fully saturated or fully unsaturated 5- or 6-membered ring, optionally having 1 to 4

heteroatoms independently selected from the group consisting of nitrogen, sulfur and oxygen;

A<sup>1</sup> for each occurrence is independently optionally substituted, in one or optionally both rings if A<sup>1</sup> is a bicyclic ring system, with up to three substituents, each substituent independently selected from the group consisting of F, Cl, Br, I, OCF<sub>3</sub>, OCF<sub>2</sub>H, CF<sub>3</sub>, CH<sub>3</sub>, OCH<sub>3</sub>, -OX<sup>6</sup>,  
-C(O)N(X<sup>6</sup>)(X<sup>6</sup>), -C(O)OX<sup>6</sup>, oxo, (C<sub>1</sub>-C<sub>6</sub>)alkyl, nitro, cyano, benzyl,  
-S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl, 1H-tetrazol-5-yl, phenyl, phenoxy, phenylalkyloxy, halophenyl, methylenedioxy, -N(X<sup>6</sup>)(X<sup>6</sup>), -N(X<sup>6</sup>)C(O)(X<sup>6</sup>), -SO<sub>2</sub>N(X<sup>6</sup>)(X<sup>6</sup>),  
-N(X<sup>6</sup>)SO<sub>2</sub>-phenyl, -N(X<sup>6</sup>)SO<sub>2</sub>X<sup>6</sup>, -CONX<sup>11</sup>X<sup>12</sup>, -SO<sub>2</sub>NX<sup>11</sup>X<sup>12</sup>, -NX<sup>6</sup>SO<sub>2</sub>X<sup>12</sup>,  
-NX<sup>6</sup>CONX<sup>11</sup>X<sup>12</sup>, -NX<sup>6</sup>SO<sub>2</sub>NX<sup>11</sup>X<sup>12</sup>, -NX<sup>6</sup>C(O)X<sup>12</sup>, imidazolyl, thiazolyl and tetrazolyl, provided that if A<sup>1</sup> is optionally substituted with methylenedioxy then it can only be substituted with one methylenedioxy;

where X<sup>11</sup> is hydrogen or optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl;

the optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl defined for X<sup>11</sup> is optionally independently substituted with phenyl, phenoxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, -S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl, 1 to 5 halogens, 1 to 3 hydroxy, 1 to 3 (C<sub>1</sub>-C<sub>10</sub>)alkanoyloxy or 1 to 3 (C<sub>1</sub>-C<sub>6</sub>)alkoxy;

X<sup>12</sup> is hydrogen, (C<sub>1</sub>-C<sub>6</sub>)alkyl, phenyl, thiazolyl, imidazolyl, furyl or thienyl, provided that when X<sup>12</sup> is not hydrogen, X<sup>12</sup> is optionally substituted with one to three substituents independently selected from the group consisting of Cl, F, CH<sub>3</sub>, OCH<sub>3</sub>, OCF<sub>3</sub> and CF<sub>3</sub>;

or X<sup>11</sup> and X<sup>12</sup> are taken together to form -(CH<sub>2</sub>)<sub>r</sub>-L<sup>1</sup>-(CH<sub>2</sub>)<sub>r</sub>;

where L<sup>1</sup> is C(X<sup>2</sup>)(X<sup>2</sup>), O, S(O)<sub>m</sub> or N(X<sup>2</sup>);

r for each occurrence is independently 1, 2 or 3;

X<sup>2</sup> for each occurrence is independently hydrogen, optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl, or optionally substituted (C<sub>3</sub>-C<sub>7</sub>)cycloalkyl, where the optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl and optionally substituted (C<sub>3</sub>-C<sub>7</sub>)cycloalkyl in the definition of X<sup>2</sup> are optionally independently substituted with -S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl, -C(O)OX<sup>3</sup>, 1 to 5 halogens or 1-3 OX<sup>3</sup>;

X<sup>3</sup> for each occurrence is independently hydrogen or (C<sub>1</sub>-C<sub>6</sub>)alkyl;

X<sup>6</sup> is independently hydrogen, optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>2</sub>-C<sub>6</sub>)halogenated alkyl, optionally substituted (C<sub>3</sub>-C<sub>7</sub>)cycloalkyl, (C<sub>3</sub>-C<sub>7</sub>)-halogenatedcycloalkyl, where optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl and optionally substituted (C<sub>3</sub>-C<sub>7</sub>)cycloalkyl in the definition of X<sup>6</sup> is optionally independently substituted by 1 or 2 (C<sub>1</sub>-C<sub>4</sub>)alkyl, hydroxyl, (C<sub>1</sub>-C<sub>4</sub>)alkoxy, carboxyl, CONH<sub>2</sub>, -S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl, carboxylate (C<sub>1</sub>-C<sub>4</sub>)alkyl ester, or 1H-tetrazol-5-yl; or

when there are two  $X^6$  groups on one atom and both  $X^6$  are independently (C<sub>1</sub>-C<sub>6</sub>)alkyl, the two (C<sub>1</sub>-C<sub>6</sub>)alkyl groups may be optionally joined and, together with the atom to which the two  $X^6$  groups are attached, form a 4- to 9- membered ring optionally having oxygen, sulfur or NX<sup>7</sup>;

$X^7$  is hydrogen or (C<sub>1</sub>-C<sub>6</sub>)alkyl optionally substituted with hydroxyl; and

m for each occurrence is independently 0, 1 or 2;

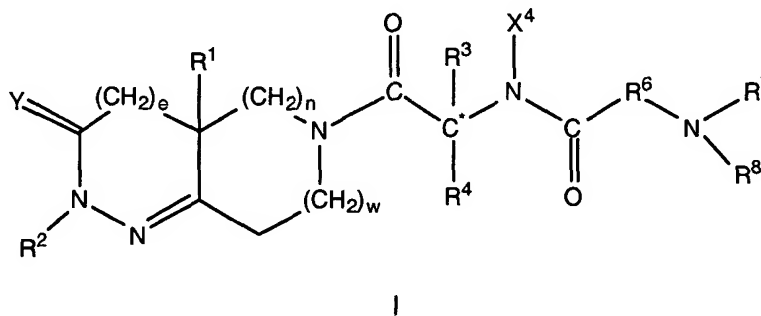
with the proviso that:

$X^6$  and  $X^{12}$  cannot be hydrogen when it is attached to C(O) or SO<sub>2</sub> in the form C(O) $X^6$ , C(O) $X^{12}$ , SO<sub>2</sub> $X^6$  or SO<sub>2</sub> $X^{12}$ ; and

when R<sup>6</sup> is a bond then L is N(X<sup>2</sup>) and each r in the definition -(CH<sub>2</sub>)<sub>r</sub>-L-(CH<sub>2</sub>)<sub>r</sub>- is independently 2 or 3.

Claims 15-25 (canceled)

26. (original) A method of treating sleep disorders in a mammal suffering from sleep disorders comprising administering to said mammal an effective amount of a compound of formula I



or the stereoisomeric mixtures, diastereomerically enriched, diastereomerically pure, enantiomerically enriched or enantiomerically pure isomers, or the pharmaceutically acceptable salts and prodrugs thereof,

wherein

e is 0 or 1;

n and w are each independently 0, 1 or 2;

provided that w and n cannot both be 0 at the same time;

Y is oxygen or sulfur;

R<sup>1</sup> is hydrogen, -CN, -(CH<sub>2</sub>)<sub>q</sub>N(X<sup>6</sup>)C(O) $X^6$ , -(CH<sub>2</sub>)<sub>q</sub>N(X<sup>6</sup>)C(O)(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>,

-(CH<sub>2</sub>)<sub>q</sub>N(X<sup>6</sup>)SO<sub>2</sub>(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>N(X<sup>6</sup>)SO<sub>2</sub> $X^6$ , -(CH<sub>2</sub>)<sub>q</sub>N(X<sup>6</sup>)C(O)N(X<sup>6</sup>)(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>,

-(CH<sub>2</sub>)<sub>q</sub>N(X<sup>6</sup>)C(O)N(X<sup>6</sup>)( $X^6$ ), -(CH<sub>2</sub>)<sub>q</sub>C(O)N(X<sup>6</sup>)( $X^6$ ), -(CH<sub>2</sub>)<sub>q</sub>C(O)N(X<sup>6</sup>)(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>,

$-(CH_2)_qC(O)OX^6$ ,  $-(CH_2)_qC(O)O(CH_2)_tA^1$ ,  $-(CH_2)_qOX^6$ ,  $-(CH_2)_qOC(O)X^6$ ,  
 $-(CH_2)_qOC(O)(CH_2)_tA^1$ ,  $-(CH_2)_qOC(O)N(X^6)(CH_2)_tA^1$ ,  $-(CH_2)_qOC(O)N(X^6)(X^6)$ ,  
 $-(CH_2)_qC(O)X^6$ ,  $-(CH_2)_qC(O)(CH_2)_tA^1$ ,  $-(CH_2)_qN(X^6)C(O)OX^6$ ,  
 $-(CH_2)_qN(X^6)SO_2N(X^6)(X^6)$ ,  $-(CH_2)_qS(O)_mX^6$ ,  $-(CH_2)_qS(O)_m(CH_2)_tA^1$ ,  
 $-(C_1-C_{10})alkyl$ ,  $-(CH_2)_tA^1$ ,  $-(CH_2)_q-(C_3-C_7)cycloalkyl$ ,  $-(CH_2)_q-Y^1-(C_1-C_6)alkyl$ ,  
 $-(CH_2)_q-Y^1-(CH_2)_tA^1$  or  $-(CH_2)_q-Y^1-(CH_2)_t-(C_3-C_7)cycloalkyl$ ;

where the alkyl and cycloalkyl groups in the definition of  $R^1$  are optionally substituted with  $(C_1-C_4)alkyl$ , hydroxyl,  $(C_1-C_4)alkoxy$ , carboxyl,  $-CONH_2$ ,

$-S(O)_m(C_1-C_6)alkyl$ ,  $-CO_2(C_1-C_4)alkyl$  ester, 1H-tetrazol-5-yl or 1, 2 or 3 fluoro;

$Y^1$  is O,  $S(O)_m$ ,  $-C(O)NX^6$ ,  $-CH=CH-$ ,  $-C\equiv C-$ ,  $-N(X^6)C(O)-$ ,  $-C(O)NX^6$ ,

$-C(O)O-$ ,  $-OC(O)N(X^6)-$  or  $-OC(O)-$ ;

$q$  is 0, 1, 2, 3 or 4;

$t$  is 0, 1, 2 or 3;

said  $(CH_2)_q$  group and  $(CH_2)_t$  group may each be optionally substituted with hydroxyl,  $(C_1-C_4)alkoxy$ , carboxyl,  $-CONH_2$ ,  $-S(O)_m(C_1-C_6)alkyl$ ,

$-CO_2(C_1-C_4)alkyl$  ester, 1H-tetrazol-5-yl, 1, 2 or 3 fluoro, or 1 or 2  $(C_1-C_4)alkyl$ ;

$R^2$  is hydrogen,  $(C_1-C_8)alkyl$ ,  $-(C_0-C_3)alkyl-(C_3-C_8)cycloalkyl$ ,  $-(C_1-C_4)alkyl-A^1$  or  $A^1$ ;

where the alkyl groups and the cycloalkyl groups in the definition of  $R^2$  are optionally substituted with hydroxyl,  $-C(O)OX^6$ ,  $-C(O)N(X^6)(X^6)$ ,  $-N(X^6)(X^6)$ ,

$-S(O)_m(C_1-C_6)alkyl$ ,  $-C(O)A^1$ ,  $-C(O)(X^6)$ ,  $CF_3$ , CN or 1, 2 or 3 halogen;

$R^3$  is  $A^1$ ,  $(C_1-C_{10})alkyl$ ,  $-(C_1-C_6)alkyl-A^1$ ,  $-(C_1-C_6)alkyl-(C_3-C_7)cycloalkyl$ ,

$-(C_1-C_5)alkyl-X^1-(C_1-C_5)alkyl$ ,  $-(C_1-C_5)alkyl-X^1-(C_0-C_5)alkyl-A^1$  or

$-(C_1-C_5)alkyl-X^1-(C_1-C_5)alkyl-(C_3-C_7)cycloalkyl$ ;

where the alkyl groups in the definition of  $R^3$  are optionally substituted with

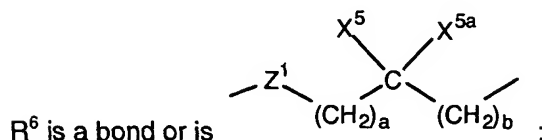
$-S(O)_m(C_1-C_6)alkyl$ ,  $-C(O)OX^3$ , 1, 2, 3, 4 or 5 halogens, or 1, 2 or 3  $OX^3$ ;

$X^1$  is O,  $S(O)_m$ ,  $-N(X^2)C(O)-$ ,  $-C(O)N(X^2)-$ ,  $-OC(O)-$ ,  $-C(O)O-$ ,  $-CX^2=CX^2-$ ,

$-N(X^2)C(O)O-$ ,  $-OC(O)N(X^2)-$  or  $-C\equiv C-$ ;

$R^4$  is hydrogen,  $(C_1-C_6)alkyl$  or  $(C_3-C_7)cycloalkyl$ , or  $R^4$  is taken together with  $R^3$  and the carbon atom to which they are attached and form  $(C_5-C_7)cycloalkyl$ ,  $(C_5-C_7)cycloalkenyl$ , a partially saturated or fully saturated 4- to 8-membered ring having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur and nitrogen, or is a bicyclic ring system consisting of a partially saturated or fully saturated 5- or 6-membered ring, fused to a partially saturated, fully unsaturated or fully saturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur and oxygen;

X<sup>4</sup> is hydrogen or (C<sub>1</sub>-C<sub>6</sub>)alkyl or X<sup>4</sup> is taken together with R<sup>4</sup> and the nitrogen atom to which X<sup>4</sup> is attached and the carbon atom to which R<sup>4</sup> is attached and form a five to seven membered ring;



where a and b are independently 0, 1, 2 or 3;

X<sup>5</sup> and X<sup>5a</sup> are each independently selected from the group consisting of hydrogen, trifluoromethyl, A<sup>1</sup> and optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl;

the optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl in the definition of X<sup>5</sup> and X<sup>5a</sup> is optionally substituted with a substituent selected from the group consisting of A<sup>1</sup>, OX<sup>2</sup>, -S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl, -C(O)OX<sup>2</sup>, (C<sub>3</sub>-C<sub>7</sub>)cycloalkyl, -N(X<sup>2</sup>)(X<sup>2</sup>) and -C(O)N(X<sup>2</sup>)(X<sup>2</sup>);

or the carbon bearing X<sup>5</sup> or X<sup>5a</sup> forms one or two alkylene bridges with the nitrogen atom bearing R<sup>7</sup> and R<sup>8</sup> wherein each alkylene bridge contains 1 to 5 carbon atoms, provided that when one alkylene bridge is formed then X<sup>5</sup> or X<sup>5a</sup> but not both may be on the carbon atom and R<sup>7</sup> or R<sup>8</sup> but not both may be on the nitrogen atom and further provided that when two alkylene bridges are formed then X<sup>5</sup> and X<sup>5a</sup> cannot be on the carbon atom and R<sup>7</sup> and R<sup>8</sup> cannot be on the nitrogen atom;

or X<sup>5</sup> is taken together with X<sup>5a</sup> and the carbon atom to which they are attached and form a partially saturated or fully saturated 3- to 7-membered ring, or a partially saturated or fully saturated 4- to 8-membered ring having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur and nitrogen;

or X<sup>5</sup> is taken together with X<sup>5a</sup> and the carbon atom to which they are attached and form a bicyclic ring system consisting of a partially saturated or fully saturated 5- or 6-membered ring, optionally having 1 or 2 heteroatoms independently selected from the group consisting of nitrogen, sulfur and oxygen, fused to a partially saturated, fully saturated or fully unsaturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur and oxygen;

Z<sup>1</sup> is a bond, O or N-X<sup>2</sup>, provided that when a and b are both 0 then Z<sup>1</sup> is not N-X<sup>2</sup> or O;

R<sup>7</sup> and R<sup>8</sup> are independently hydrogen or optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl;

where the optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl in the definition of R<sup>7</sup> and R<sup>8</sup> is optionally independently substituted with A<sup>1</sup>, -C(O)O-(C<sub>1</sub>-C<sub>6</sub>)alkyl,

-S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl, 1 to 5 halogens, 1 to 3 hydroxy, 1 to 3 -O-C(O)(C<sub>1</sub>-C<sub>10</sub>)alkyl or 1 to 3 (C<sub>1</sub>-C<sub>6</sub>)alkoxy; or

R<sup>7</sup> and R<sup>8</sup> can be taken together to form -(CH<sub>2</sub>)<sub>r</sub>-L-(CH<sub>2</sub>)<sub>r</sub>;

where L is C(X<sup>2</sup>)(X<sup>2</sup>), S(O)<sub>m</sub> or N(X<sup>2</sup>);

A<sup>1</sup> for each occurrence is independently (C<sub>5</sub>-C<sub>7</sub>)cycloalkenyl, phenyl or a partially saturated, fully saturated or fully unsaturated 4- to 8-membered ring optionally having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur and nitrogen, a bicyclic ring system consisting of a partially saturated, fully unsaturated or fully saturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur and oxygen, fused to a partially saturated, fully saturated or fully unsaturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur and oxygen;

A<sup>1</sup> for each occurrence is independently optionally substituted, in one or optionally both rings if A<sup>1</sup> is a bicyclic ring system, with up to three substituents, each substituent independently selected from the group consisting of F, Cl, Br, I, OCF<sub>3</sub>, OCF<sub>2</sub>H, CF<sub>3</sub>, CH<sub>3</sub>, OCH<sub>3</sub>, -OX<sup>6</sup>, -C(O)N(X<sup>6</sup>)(X<sup>6</sup>), -C(O)OX<sup>6</sup>, oxo, (C<sub>1</sub>-C<sub>6</sub>)alkyl, nitro, cyano, benzyl, -S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl, 1H-tetrazol-5-yl, phenyl, phenoxy, phenylalkyloxy, halophenyl, methylenedioxy, -N(X<sup>6</sup>)(X<sup>6</sup>), -N(X<sup>6</sup>)C(O)(X<sup>6</sup>), -SO<sub>2</sub>N(X<sup>6</sup>)(X<sup>6</sup>), -N(X<sup>6</sup>)SO<sub>2</sub>-phenyl, -N(X<sup>6</sup>)SO<sub>2</sub>X<sup>6</sup>, -CONX<sup>11</sup>X<sup>12</sup>, -SO<sub>2</sub>NX<sup>11</sup>X<sup>12</sup>, -NX<sup>6</sup>SO<sub>2</sub>X<sup>12</sup>, -NX<sup>6</sup>CONX<sup>11</sup>X<sup>12</sup>, -NX<sup>6</sup>SO<sub>2</sub>NX<sup>11</sup>X<sup>12</sup>, -NX<sup>6</sup>C(O)X<sup>12</sup>, imidazolyl, thiazolyl and tetrazolyl, provided that if A<sup>1</sup> is optionally substituted with methylenedioxy then it can only be substituted with one methylenedioxy;

where X<sup>11</sup> is hydrogen or optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl;

the optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl defined for X<sup>11</sup> is optionally independently substituted with phenyl, phenoxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, -S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl, 1 to 5 halogens, 1 to 3 hydroxy, 1 to 3 (C<sub>1</sub>-C<sub>10</sub>)alkanoyloxy or 1 to 3 (C<sub>1</sub>-C<sub>6</sub>)alkoxy;

X<sup>12</sup> is hydrogen, (C<sub>1</sub>-C<sub>6</sub>)alkyl, phenyl, thiazolyl, imidazolyl, furyl or thienyl, provided that when X<sup>12</sup> is not hydrogen, X<sup>12</sup> is optionally substituted with one to three substituents independently selected from the group consisting of Cl, F, CH<sub>3</sub>, OCH<sub>3</sub>, OCF<sub>3</sub> and CF<sub>3</sub>;

or X<sup>11</sup> and X<sup>12</sup> are taken together to form -(CH<sub>2</sub>)<sub>r</sub>-L<sup>1</sup>-(CH<sub>2</sub>)<sub>r</sub>;

where L<sup>1</sup> is C(X<sup>2</sup>)(X<sup>2</sup>), O, S(O)<sub>m</sub> or N(X<sup>2</sup>);

r for each occurrence is independently 1, 2 or 3;

$X^2$  for each occurrence is independently hydrogen, optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl, or optionally substituted (C<sub>3</sub>-C<sub>7</sub>)cycloalkyl, where the optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl and optionally substituted (C<sub>3</sub>-C<sub>7</sub>)cycloalkyl in the definition of  $X^2$  are optionally independently substituted with -S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl, -C(O)OX<sup>3</sup>, 1 to 5 halogens or 1-3 OX<sup>3</sup>;

$X^3$  for each occurrence is independently hydrogen or (C<sub>1</sub>-C<sub>6</sub>)alkyl;

$X^6$  is independently hydrogen, optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>2</sub>-C<sub>6</sub>)halogenated alkyl, optionally substituted (C<sub>3</sub>-C<sub>7</sub>)cycloalkyl, (C<sub>3</sub>-C<sub>7</sub>)-halogenatedcycloalkyl, where optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl and optionally substituted (C<sub>3</sub>-C<sub>7</sub>)cycloalkyl in the definition of  $X^6$  is optionally independently substituted by 1 or 2 (C<sub>1</sub>-C<sub>4</sub>)alkyl, hydroxyl, (C<sub>1</sub>-C<sub>4</sub>)alkoxy, carboxyl, CONH<sub>2</sub>, -S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl, carboxylate (C<sub>1</sub>-C<sub>4</sub>)alkyl ester, or 1H-tetrazol-5-yl; or

when there are two  $X^6$  groups on one atom and both  $X^6$  are independently (C<sub>1</sub>-C<sub>6</sub>)alkyl, the two (C<sub>1</sub>-C<sub>6</sub>)alkyl groups may be optionally joined and, together with the atom to which the two  $X^6$  groups are attached, form a 4- to 9- membered ring optionally having oxygen, sulfur or NX<sup>7</sup>;

$X^7$  is hydrogen or (C<sub>1</sub>-C<sub>6</sub>)alkyl optionally substituted with hydroxyl; and

m for each occurrence is independently 0, 1 or 2;

with the proviso that:

$X^6$  and  $X^{12}$  cannot be hydrogen when it is attached to C(O) or SO<sub>2</sub> in the form C(O)X<sup>6</sup>, C(O)X<sup>12</sup>, SO<sub>2</sub>X<sup>6</sup> or SO<sub>2</sub>X<sup>12</sup>; and

when R<sup>6</sup> is a bond then L is N(X<sup>2</sup>) and each r in the definition -(CH<sub>2</sub>)<sub>r</sub>-L-(CH<sub>2</sub>)<sub>r</sub>- is independently 2 or 3.